Complete Summary

GUIDELINE TITLE

ACR Appropriateness Criteria® locally advanced breast cancer.

BIBLIOGRAPHIC SOURCE(S)

Strom EA, Yu T, Rabinovitch RA, Haffty BG, Halberg FE, Taylor ME, White JR, Cobleigh MA, Edge SB, Expert Panel on Radiation Oncology-Breast. ACR Appropriateness Criteria® locally advanced breast cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 12 p. [99 references]

GUIDELINE STATUS

This is the current release of the guideline.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Locally advanced breast cancer

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Internal Medicine
Obstetrics and Gynecology
Oncology
Radiation Oncology
Surgery

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of treatment procedures for patients with locally advanced breast cancer

TARGET POPULATION

Patients with locally advanced breast cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Surgery
    - Mastectomy
    - Breast-conservation therapy (BCT)
    - Mastectomy or BCT with axillary dissection
    - Debulking surgery
2. Radiation therapy (RT)
    - Whole breast with or without boost (no nodal RT)
    - Partial breast irradiation (no nodal RT)
    - Whole breast and supraclavicular and apical axillary nodes
    - Whole breast and supraclavicular lymph nodes (LNs) and full axilla
    - Internal mammary nodes (IMN)
    - Boost to infraclavicular region
    - Chest wall only, with or without boost
    - Chest wall, supraclavicular and apical nodes
    - Chest wall, supraclavicular fossa and full axilla
    - Boost to chest wall
    - Boost to internal mammary chain
    - Boost to supraclavicular nodes
    - Palliative RT
3. Chemotherapy
4. Endocrine therapy
5. Combined modality therapy

MAJOR OUTCOMES CONSIDERED

- Overall survival rate

- Disease-free survival
- Local recurrence rate
- Distant metastasis
- Toxicity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1–9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Locally Advanced Breast Cancer

Variant 1: 45-year-old premenopausal female, 4.5 cm infiltrating ductal carcinoma (IDC) left breast, estrogen receptor/progesterone receptor (ER/PR) (-), Her2 amplified, positron emission tomography (PET) (+) in breast, axilla and medial infraclavicular fossa. Palpable nodes in high axilla. Metastatic workup negative. Patient desires breast conservation.

Treatment	Rating	Comments
Principles of Treatment		
Initial chemotherapy	9	
Breast conservation therapy (BCT) if ≥PR to chemotherapy	8	For some patients with less than PR, breast conservation may be appropriate if surgically feasible.
Initial mastectomy and axillary dissection	1	N3 status contraindicates initial surgical approach.
Initial BCT and axillary dissection	1	
Radiation Volumes (assume initial chemotherapy followed by BCT, clear margins, and axilla dissection level I-II, 8/16 LN+, highest node+)		
Whole breast only ± boost (no nodal RT)	1	
Partial breast irradiation (no nodal RT)	1	
Whole breast and supraclavicular + apical axillary nodes	9	
Whole breast and supraclavicular LNs and full axilla	7	Probably not required after a standard axillary dissection.
Internal mammary nodes (assumes breast RT given concurrently)	8	Provided caution is taken to minimize cardiac pulmonary volumes.
Boost infraclavicular region	8	Boost determined by extent of surgical resection and clinical features.
Radiation Doses (1.8-2.0 Gy/day unless specified otherwise) (assume initial chemotherapy followed by BCT, clear margins, and axilla dissection level I-II, 8/16 LN+, highest node+)		
Whole breast: 42.5 Gy (16 fractions)	1	
Whole breast: 45-50 Gy	9	

Treatment	Rating	Comments
Total dose to breast tumor bed: 45-50 Gy	1	
Total dose to breast tumor bed: 60-66 Gy	9	
Total dose to supraclavicular fossa and axillary apex: 45-50 Gy	9	
Total dose to supraclavicular fossa and axillary apex: 60 Gy	1	
Total dose to medial infraclavicular nodes: ≥60Gy	8	Gross tumor may require higher doses. Higher doses risk brachial plexus. CT planning recommended.
Full axilla: 45-50 Gy	7	
IMN: 45-50 Gy	7	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 2: 40-year-old woman, 4 cm primary with diffuse suspicious microcalcifications in breast, direct skin invasion, satellite skin nodule, matted axilla (N2), ER (+)/PR (−), Her2 (−). Metastatic workup negative.

Treatment	Rating	Comments
Principles of Treatment		
Initial chemotherapy	9	
Mastectomy if response to initial chemotherapy	9	
Initial endocrine therapy	2	Only if cytotoxic therapy contraindicated or on a clinical trial.
Initial surgery	1	
Initial breast and nodal RT	1	
BCT if response to initial	1	

Treatment	Rating	Comments
chemotherapy		
Radiation Volumes (assume chemotherapy, mastectomy, axillary dissection level I-II, 3/16 LN+)		
Chest wall only ± boost (no nodal RT)	1	
Chest wall, supraclavicular and apical nodes	9	
Chest wall, supraclavicular fossa + full axilla	7	
Internal mammary nodes (assumes chest wall RT)	8	
Boost to chest wall	9	
Radiation Doses (1.8–2.0 Gy/day unless specified otherwise) (assume chemotherapy, mastectomy, clear margins, and axilla dissection level I-II, 3/16 LN+)		
Chest wall: 45-50 Gy	9	
Total dose to chest wall including boost: 60-66 Gy	9	
Supraclavicular and axillary nodes: 45-50 Gy	9	
Full axilla: 45-50 Gy	7	
IMN: 45-50 Gy	7	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 3: 80-year-old woman, 4 cm primary, direct skin invasion, satellite nodule, matted axilla (N2), strongly ER/PR (+), Her2 (–). Metastatic workup negative. Medically fit.

Treatment	Rating	Comments

Treatment	Rating	Comments
Treatment Modalities		
Initial endocrine therapy	9	Both are considered equally appropriate.
Initial chemotherapy	9	Both are considered equally appropriate.
Initial surgery	1	
Initial breast and nodal RT	1	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 4: 50-year-old woman, T3N2M0 disease, with clinical CR post 4-cycle multidrug chemotherapy. ER/PR (–), Her2 (–). Does not desire BCT.

Treatment	Rating	Comments
Treatment Modalities		
Mastectomy and axillary dissection	9	
Additional chemotherapy	9	Would complete all chemotherapy up front. Depends on what drugs are used
Postmastectomy RT	9	
No surgery: RT + chemotherapy	1	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 5: 38-year-old woman, T4 inflammatory, N1 disease, no response post 3-cycle multidrug chemotherapy. ER/PR (–), Her2 (–). Metastatic workup negative.

Treatment	Rating	Comments
Principles of Treatment		
Change chemotherapy; if no response, proceed	9	

Treatment	Rating	Comments
to RT		
Change chemotherapy; if response, mastectomy	9	
Change chemotherapy; if no response, pre-op chemoradiation (radiosensitizing chemotherapy)	7	
Immediate mastectomy/axillary dissection	1	
Radiotherapy (assume sufficient response to be operable with clear margins)		
Standard fractionation (1.8-2.0 Gy)	9	
Accelerated fractionation (1.5 Gy BID)	7	
Dose to central chest wall: 45-50 Gy	9	
Total dose to chest wall including boost: 60-66 Gy	9	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 6: 42-year-old woman, T2N1 (clin), M0 left breast cancer, Her2 amplified. Status post mastectomy with 11/12 (+) nodes and reconstruction plus chemotherapy, no evidence of disease. Will receive trastuzumab for one year.

Treatment	Rating	Comments
Principles of Treatment		
Chest wall RT	9	
Supraclavicular RT	9	

Treatment	Rating	Comments
Attempt to exclude all heart from RT volume	9	
Full axilla RT	7	
IMN RT	7	
RT dose adjustment (decrease) due to reconstruction	5	
Discontinue trastuzumab during radiotherapy	1	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 7: 57-year-old woman, triple negative IDC, status post-mastectomy: 3.5 cm inner quadrant primary, 7/12 LN (+). Focally positive deep margin. PET (+) IMC and S/C nodes. Adjuvant anthracycline and taxane, with normalization of PET findings. Metastatic workup negative.

Treatment	Rating	Comments
Radiation Volumes		
Chest wall only ± boost	1	
Supraclavicular + apical nodes (assumes chest wall RT also)	9	
Full axilla (assumes chest wall RT also)	7	
Internal mammary nodes (assumes chest wall RT)	9	
Boost to IMC	8	
Boost supraclavicular nodes	8	
Radiation Doses		
Total dose to chest wall	1	

Treatment	Rating	Comments
including boost: 45-50 Gy		
Total dose to chest wall including boost: 60 Gy	2	
Total dose to chest wall including boost: 64-66 Gy	9	Clinical circumstance may require higher dose.
Total dose to supraclavicular fossa including boost: 45-50 Gy	9	
Total dose to supraclavicular fossa including boost: 60-66 Gy	9	
Total dose to entire IMN chain: 45-50 Gy	9	
Total dose to entire IMN chain: 60-66 Gy	9	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 8: 55-year-old woman with neglected primary. Large, fungating lesion and matted axilla. ER (−) /PR (+), Her2 (−). Metastatic workup negative. Not operable after three chemo regimens, including anthracyclines and taxanes.

Treatment	Rating	Comments
Principles of Treatment		
Switch to endocrine therapy	9	
Switch to 4th line chemotherapy	3	Appropriate in phase I clinical trial.
Debulking surgery with anticipated + margins	3	
Palliative radiation (30-45 Gy)	No consensus	May be appropriate in selected clinical circumstances.

Treatment	Rating	Comments
Concurrent chemoradiation	No consensus	May be appropriate in selected clinical circumstances.
Preoperative RT (50-54 Gy)	No consensus	May be appropriate in selected clinical circumstances.
Definitive RT to ≥70 Gy	No consensus	May be appropriate in selected clinical circumstances.
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Summary

Patients with locally advanced breast cancer (LABC) have a high risk for both local-regional recurrence (LRR) and distant metastasis (DM). Proper initial imaging of the breast and nodal beds is essential for both staging and RT planning. There are only a few randomized trials that specifically examined the role of radiation in LABC patients. Preferred techniques and clinical target volumes and the optimum doses to these regions have not been prospectively studied for advanced breast cancer. However, trimodality therapy with chemotherapy, surgery, and radiation seems to accomplish the best outcome. In fact, breast conservation can be achieved in a select population of patients who have a good response to neoadjuvant chemotherapy.

Abbreviations

- BCT, breast conservation therapy
- BID, twice a day
- CT, computed tomography
- ER, estrogen receptor
- IDC, infiltrating ductal carcinoma
- IMC, internal mammary chain
- IMN, internal mammary (lymph) node
- LN, lymph node
- PET, positron emission tomography
- PR, progesterone receptor
- RT, radiation therapy
- S/C, supraclavicular

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Selection of appropriate treatment procedures for patients with locally advanced breast cancer

POTENTIAL HARMS

Many common toxicities, such as radiation dermatitis, occur during the course of irradiation for locally advanced breast cancer. However, one major toxicity noted in the older studies was an increase in cardiovascular mortality in patients treated with postmastectomy radiation therapy (RT). Analyzing data from the Surveillance, Epidemiology and End Results (SEER) database in early breast cancer patients, patients who were treated to the left breast had progressively increasing risk for ischemic mortality with longer time interval from the RT. This was only significant for patients treated before 1982. No difference in 15-year mortality from ischemic events was seen between patients who received left breast versus right breast RT when the radiation was delivered after 1980.

CONTRAINDICATIONS

CONTRAINDICATIONS

- In patients with inflammatory breast cancer mastectomy is generally considered to be contraindicated although reports have shown an improvement in local control when mastectomy was added, but only in patients who have good response to preoperative chemotherapy.
- N3 status contraindicates initial surgical approach.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been

considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Strom EA, Yu T, Rabinovitch RA, Haffty BG, Halberg FE, Taylor ME, White JR, Cobleigh MA, Edge SB, Expert Panel on Radiation Oncology-Breast. ACR Appropriateness Criteria® locally advanced breast cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 12 p. [99 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology–Breast

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Eric A. Strom, MD; Tse-Kuan Yu, MD, PhD; Rachel Abrams Rabinovitch, MD; Bruce G. Haffty, MD; Francine E. Halberg, MD; Marie E. Taylor, MD; Julia R. White, MD; Melody A. Cobleigh, MD; Stephen B. Edge, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on September 10, 2009.

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